■ HIP

Which factors influence the rate of failure following metal-on-metal hip arthroplasty revision surgery performed for adverse reactions to metal debris?

AN ANALYSIS FROM THE NATIONAL JOINT REGISTRY FOR ENGLAND AND WALES

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Aims
To determine the outcomes following revision surgery of metal-on-metal hip arthroplasties (MoMHA) performed for adverse reactions to metal debris (ARMD), and to identify factors predictive of re-revision.

Patients and Methods
We performed a retrospective observational study using National Joint Registry (NJR) data on 2535 MoMHAs undergoing revision surgery for ARMD between 2008 and 2014. The outcomes studied following revision were intra-operative complications, mortality and re-revision surgery. Predictors of re-revision were identified using competing-risk regression modelling.

Results
Intra-operative complications occurred in 40 revisions (1.6%). The cumulative five-year patient survival rate was 95.9% (95% confidence intervals (CI) 92.3 to 97.8). Re-revision surgery was performed in 192 hips (7.6%). The cumulative five-year implant survival rate was 89.5% (95% CI 87.3 to 91.3). Predictors of re-revision were high body mass index at revision (subhazard ratio (SHR) 1.06 per kg/m^2 increase, 95% CI 1.02 to 1.09), modular component only revisions (head and liner with or without taper adapter; SHR 2.01, 95% CI 1.19 to 3.38), ceramic-on-ceramic revision bearings (SHR 1.86, 95% CI 1.23 to 2.80), and acetabular bone grafting (SHR 2.10, 95% CI 1.43 to 3.07). These four factors remained predictive of re-revision when the missing data were imputed.

Conclusion
The short-term risk of re-revision following MoMHA revision surgery performed for ARMD was comparable with that reported in the NJR following all-cause non-MoMHA revision surgery. However, the factors predictive of re-revision included those which could be modified by the surgeon, suggesting that rates of failure following ARMD revision may be reduced further.

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The early observations following revision surgery of metal-on-metal hip arthroplasty (MoMHA) performed for adverse reactions to metal debris (ARMD) suggested a high prevalence of short-term complications and re-revisions.[1,2] Following revision for ARMD, the most frequent modes of subsequent failure have been reported as dislocation, recurrent ARMD and acetabular loosening.[3] In addition, implant survival and patient-reported outcomes have been inferior for MoMHAs revised for ARMD compared with other indications, and compared with matched patients undergoing primary total hip arthroplasty (THA).[1] This is most likely to be related to the potentially destructive nature of ARMD.[1,4,5] Furthermore, the ten-year implant rate of survival following ARMD revision was recently reported to be only 56%, with surviving patients continuing to have poor patient-reported outcomes at extended follow-up.[6]

Some studies have assessed factors predictive of poor outcomes following revision for ARMD.[5,7,8] However, these studies were small and therefore underpowered for the identification of prognostic factors. There are still many

MoMHA patients who are likely to require revision surgery for ARMD in the future.[3] Therefore, it is important that surgeons have information concerning the expected outcomes in order to appropriately counsel patients regarding any potential risks. Furthermore, knowledge of prognostic factors will assist surgeons when making decisions regarding the reconstructive procedure and post-operative surveillance. Large cohort studies are ideally suited to answer these important clinical questions. The National Joint Registry (NJR) for England and Wales was established in 2002 (and began collecting data on hip and knee joint replacements in April 2003) to facilitate the early identification of poorly performing implants.[9] It is the largest arthroplasty registry in the world, and contains the details of two million joint replacement procedures.

We used NJR data to assess the outcomes following revision surgery of MoMHAs performed for ARMD, and to identify factors predictive of re-revision surgery.

Patients and Methods

A retrospective observational study was performed using all data submitted to the NJR up to 14 August 2015. This dataset included details of all primary MoMHAs (THA and hip resurfacing, HR) which subsequently underwent revision surgery for adverse soft-tissue reaction to particulate debris as recorded in the NJR between 01 June 2008 and 14 August 2014 (n = 2567). We have elected to classify this revision indication as ARMD throughout, given that this is currently the most commonly used term in the literature.[10] This dataset did not include primary MoMHAs revised to another MoMHA for non-ARMD indications (such as fracture, loosening, osteonecrosis) before subsequent revision for ARMD,[6] as we did not wish to include patients who had undergone multiple procedures. ARMD was first introduced on the NJR data capture forms as an indication for revision surgery in June 2008. The cut-off date of 14 August 2014 allowed a minimum follow-up period of one year for outcome assessment. Prior to obtaining the dataset the entire NJR database was linked with the Office for National Statistics database, which provides data on all-cause patient mortality, using unique patient identifiers.

Patients were subsequently excluded from the cohort for the following reasons: the ARMD revision was recorded in the NJR as the first stage (excision arthroplasty) of a two-stage procedure, but the second stage re-implantation procedure was absent from the NJR (18 hips excluded); the first stage was recorded as performed for ARMD, but the second stage was recorded as performed for non-ARMD indications such as infection (ten hips excluded); it was not possible to determine whether the primary MoMHA was a THA or HR from the recorded component information (four hips excluded). The final cohort for analysis included 2535 primary MoMHAs undergoing revision surgery for ARMD.

Unique patient identifiers allowed linkage of all ARMD revisions to the primary MoMHA and any future re-revisions. For all procedures, the NJR collects data on patient demographics (age, gender, body mass index (BMI), American Society of Anesthesiologists grade),[11] the surgery performed (indication, venous thromboembolism prophylaxis, surgeon grade, approach, components implanted including bearing surface, size, and fixation), and the occurrence of intra-operative complications (calcar crack, pelvic and/or femoral shaft penetration, trochanteric and/or femoral shaft fracture, and other complications). In addition, intra-operative findings are recorded for revision procedures. Patient and surgical factors relating to the ARMD revision procedure were used as covariates when assessing predictors of re-revision surgery. Outcomes of interest were intra-operative complications during ARMD revision, and all-cause mortality and all-cause re-revision surgery following ARMD revision.

Statistical analysis. All analyses were performed using Stata Version 14.2 (StataCorp LLC, College Station, Texas). The significance level for all analyses was a p-value < 0.05, with 95% confidence intervals (CI) also used. Differences in patient and surgical factors between re-revised and non-re-revised hips were assessed using either unpaired *t*-tests or the Wilcoxon rank-sum test (numerical data), and either the chi-squared test or Fisher's exact test (categorical data). Cumulative patient and implant survival rates following ARMD revision surgery were determined using the Kaplan-Meier method. The endpoint for implant survival was re-revision surgery (removal or exchange of any component). Patients not undergoing re-revision who remained alive were censored on the study end date (14 August 2015).

Fine and Gray[12] competing-risk regression modelling was used to identify predictors of re-revision surgery as mortality can be considered a competing risk. Univariable models explored the association between each predictor and re-revision surgery. Linearity of continuous predictors with outcome (re-revision) was assessed using fractional polynomials, with data grouped if effects were non-linear. The proportional subhazards assumption was satisfied for all predictors. The final multivariable competing-risk regression model was developed using stepwise selection methods. The p-values for the removal and inclusion of predictors in the final multivariable model were $p \geq 0.20$ and $p < 0.10$, respectively. The discriminatory ability of the final multivariable model for distinguishing between hips that did or did not undergo re-revision surgery was analysed using the concordance (c) statistic. The c statistic (range 0 to 1; useful prognostic models = 0.60 to 0.85) provides a global assessment of fit for the survival model, and is equivalent to the area under a receiver operating characteristic curve.[13,14]

There were four covariates with missing data (BMI n = 682; revision procedure n = 5; revision femoral head size n = 29; revision bearing surface n = 119). As a sensitivity analysis, regression models were repeated using a complete dataset where missing data were imputed.

Table I. Patient and surgical factors for all metal-on-metal hip arthroplasties revised for adverse reactions to metal debris (ARMD) with hips not undergoing re-revision surgery compared with those undergoing re-revision surgery

Covariate	All ARMD hip revisions (n = 2535) (100%)	ARMD hip revisions not undergoing re-revision surgery (n = 2343) (92.4%)	ARMD hip revisions undergoing re-revision surgery (n = 192) (7.6%)	p-value
Gender, n (%)				
Female	1509 *(59.5)*	1388 *(59.2)*	121 *(63.0)*	0.305
Age at revision (yrs)				
Mean (SD)	63.6 (10.1)	63.7 (10.0)	62.3 (11.0)	0.1045
BMI (kg/m²)*				
Mean (SD)	29.0 (5.1)	28.9 (5.1)	30.1 (5.7)	**0.0179**
Bilateral revisions for ARMD, n (%)	224 *(8.8)*	206 *(8.8)*	18 *(9.4)*	0.784
Primary arthroplasty, n (%)				
THA	1716 *(67.7)*	1572 *(67.1)*	144 *(75.0)*	**0.024**
HR	819 *(32.3)*	771 *(32.9)*	48 *(25.0)*	
Primary femoral head size (mm), n (%)				
≤ 36	470 *(18.5)*	429 *(18.3)*	41 *(21.4)*	0.737
38 to 44	751 *(29.6)*	696 *(29.7)*	55 *(28.7)*	
46 to 50	1102 *(43.5)*	1020 *(43.5)*	82 *(42.7)*	
≥ 52	212 *(8.4)*	198 *(8.5)*	14 *(7.3)*	
Time from primary to revision (yrs)				
Mean (SD)	5.2 (1.8)	5.3 (1.8)	4.7 (1.9)	**< 0.0001**
ASA grade at revision, n (%)				
1	476 *(18.8)*	438 *(18.7)*	38 *(19.8)*	0.769
2	1827 *(72.1)*	1688 *(72.0)*	139 *(72.4)*	
3 or above	232 *(9.2)*	217 *(9.3)*	15 *(7.8)*	
VTE – chemical, n (%)				
LMWH (+/-other)	1309 *(51.6)*	1219 *(52.0)*	90 *(46.9)*	0.167
Aspirin only	68 *(2.7)*	62 *(2.7)*	6 *(3.1)*	
Other	922 *(36.4)*	852 *(36.4)*	70 *(36.5)*	
None	236 *(9.3)*	210 *(9.0)*	26 *(13.5)*	
VTE – mechanical, n (%)				
Any *vs* none	2447 *(96.5)*	2263 *(96.6)*	184 *(95.8)*	0.584
Number of ARMD hip revision procedures performed by each of 237 centres				
Median (range)	28 (1 to 169)	28 (1 to 169)	34 (1 to 169)	0.0532
Revision surgeon grade, n (%)				
Consultant *vs* other	2430 *(95.9)*	2247 *(95.9)*	181 *(95.3)*	0.693
Surgical approach				
Posterior *vs* other	2084 *(82.2)*	1929 *(82.3)*	155 *(80.7)*	0.577
Revision indications/intra-operative findings, n (%)				
ARMD only	1604 *(63.3)*	1474 *(62.9)*	130 *(67.7)*	0.185
2 to 6 indications	931 *(36.7)*	869 *(37.1)*	62 *(32.3)*	
ARMD	2535 *(100)*	2343 *(100)*	192 *(100)*	NA
Pain	554 *(21.9)*	522 *(22.3)*	32 *(16.7)*	0.070
Aseptic loosening (any)	219 *(8.6)*	206 *(8.8)*	13 *(6.8)*	0.338
Acetabular loosening	125 *(4.9)*	118 *(5.0)*	7 *(3.7)*	0.392
Femoral loosening	112 *(4.4)*	105 *(4.5)*	7 *(3.7)*	0.588
Osteolysis (any)	177 *(6.9)*	166 *(7.1)*	11 *(5.7)*	0.479
Acetabular osteolysis	110 *(4.3)*	104 *(4.4)*	6 *(3.1)*	0.390
Femoral osteolysis	101 *(4.0)*	95 *(4.1)*	6 *(3.1)*	0.527
Other abnormal findings	85 *(3.4)*	81 *(3.5)*	‡	0.405
Implant malalignment	79 *(3.1)*	76 *(3.2)*	‡	0.278
Acetabular component wear	43 *(1.7)*	40 *(1.7)*	‡	1.00
Fracture	43 *(1.7)*	39 *(1.7)*	‡	0.563
Dislocation/subluxation	37 *(1.5)*	29 *(1.2)*	8 *(4.2)*	**0.005**
Infection	22 *(0.9)*	19 *(0.8)*	‡	0.230
Incorrect implant size	9 *(0.4)*	8 *(0.3)*	‡	0.508
Liner dissociation	9 *(0.4)*	9 *(0.4)*	0 *(0)*	1.00
Implant fracture	6 *(0.2)*	6 *(0.3)*	0 *(0)*	1.00
Revision procedure,* n (%)				
All components revised	1032 *(40.8)*	968 *(41.4)*	64 *(33.5)*	**0.031**
Acetabular component (+/- head +/- liner +/- taper adapter)	1163 *(46.0)*	1071 *(45.8)*	92 *(48.2)*	
Femoral component (+/- head +/- liner +/- taper adapter)	78 *(3.1)*	73 (3.1)	‡	
Modular components only†	257 *(10.2)*	227 *(9.7)*	30 *(15.7)*	
Revision femoral head size (mm),* n (%)				
Mean (SD)	34.3 (3.2)	34.2 (3.2)	34.4 (3.4)	0.418
Range	22.25 to 48	22.25 to 44	22.25 to 48	
< 36	882 *(35.3)*	820 *(35.5)*	62 *(33.0)*	0.751
36	1486 *(59.5)*	1371 *(59.4)*	115 *(61.2)*	
> 36	130 *(5.2)*	119 *(5.2)*	11 *(5.9)*	
Revision bearing surface,* n (%)				
CoP	1104 *(45.7)*	1040 *(46.5)*	64 *(35.4)*	**0.017**
CoC	765 *(31.7)*	693 *(31.0)*	72 *(39.8)*	
MoP	533 *(22.1)*	488 *(21.8)*	45 *(24.9)*	
CoM, MoM or MoC	14 (0.6)	14 *(0.6)*	0 *(0)*	
Acetabular component fixation, n (%)				
Cementless	1919 *(87.5)*	1780 *(87.3)*	139 *(89.1)*	0.522
Cemented	275 *(12.5)*	258 *(12.7)*	17 *(10.9)*	
Femoral component fixation, n (%)				
Cementless	723 *(65.3)*	674 *(64.9)*	49 *(71.0)*	0.299
Cemented	385 *(34.8)*	365 *(35.1)*	20 *(29.0)*	
Bone graft (femoral), n (%)	76 *(3.0)*	71 *(3.0)*	‡	0.739
Bone graft (acetabular), n (%)	509 *(20.1)*	457 *(19.5)*	52 *(27.1)*	**0.012**

*missing data for stated number of hips: BMI (n = 682); revision procedure (n = 5); revision femoral head size (n = 29); revision bearing surface (n = 119)
†involves revision of the femoral head and liner, with or without the use of a taper adapter
‡data suppressed due to small count within the cell. The actual number was between 1 and 5
Statistically significant differences between the re-revised and non-re-revised hips ($p < 0.05$) are highlighted in bold text
All numerical data were compared using unpaired *t*-tests, apart from the number of ARMD hip revision procedures performed by each centre, which was compared using the Wilcoxon rank-sum test. All categorical data were compared using the chi-squared test, apart from the following covariates, which were compared using Fisher's exact test: certain revision indications (other abnormal findings; implant malalignment; acetabular component wear; fracture; infection; incorrect implant size; liner dissociation; implant fracture), revision procedure, revision bearing surface, and bone graft (femoral)
SD, standard deviation; BMI, body mass index; THA, total hip arthroplasty; HR, hip resurfacing; ASA, American Society of Anesthesiologists; VTE, venous thromboembolism; LMWH, low molecular weight heparin; CoP, ceramic-on-polyethylene; CoC, ceramic-on-ceramic; MoP, metal-on-polyethylene; CoM, ceramic-on-metal; MoM, metal-on-metal; MoC, metal-on-ceramic; NA, not applicable

Multiple imputation is an accepted statistical method for managing missing data.[15] In total, 50 complete datasets were imputed, with data assumed to be missing at random. Imputation models included all other covariates from the regression analyses with complete data available and the study outcome (Nelson-Aalen estimate, and whether the hip was re-revised), given that all of these factors carried information about the missing values.

Results

Intra-operative complications. Of the 2535 MoMHAs revised for ARMD (Table I), intra-operative complications

Table II. Indications for metal-on-metal hip arthroplasties undergoing re-revision surgery following revision surgery performed for adverse reactions to metal debris (n = 192)

Re-revision indications and intra-operative findings	Events, n (%)
Overall	291 causes in 192 re-revised hips
Hips with one indication	121 (*63.0*)
Hips with two to four indications	71 (*37.0*)
Specific indications	
Pain	52 (*27.1*)
Adverse reactions to metal debris	48 (*25.0*)
Dislocation/subluxation	43 (*22.4*)
Deep infection	31 (*16.1*)
Aseptic loosening – acetabular	29 (*15.1*)
Aseptic loosening – femoral	15 (*7.8*)
Implant malalignment – acetabular	15 (*7.8*)
Osteolysis – femoral	10 (*5.2*)
Other indication	10 (*5.2*)
Periprosthetic fracture – femoral	8 (*4.2*)
Periprosthetic fracture – acetabular	8 (*4.2*)
Acetabular component wear	8 (*4.2*)
Other (including femoral malalignment, implant fracture, and liner dissociation)	8 (*4.2*)
Osteolysis – acetabular	6 (*3.1*)

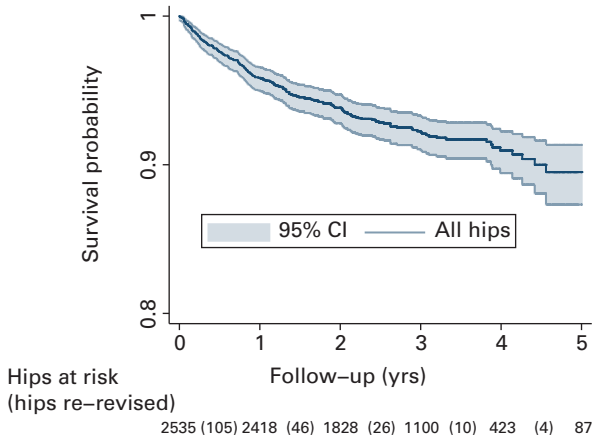

Fig. 1

Kaplan-Meier cumulative implant survival rate following revision surgery performed for adverse reactions to metal debris at up to five years. The shaded area represents the respective upper and lower limits of the 95% confidence intervals (CIs). Risk table indicates the number of hips at risk at one-year intervals, with the corresponding number in brackets detailing the number of hips undergoing re-revision surgery during each one-year interval. The one re-revision which was performed more than five years following revision surgery is not included in the risk table. The cumulative five-year implant rate of survival was 89.5% (95% CI 87.3 to 91.3).

occurred in 40 hips (1.6%). The most common complications were fractures of the calcar (n = 11, 27.5%) and greater trochanter (n = 8, 20.0%).

Patient mortality. Overall mortality following revision surgery was 1.6% (n = 41). The mean time from ARMD revision to death was 1.9 years (0.1 to 5.9); no patient who died during the follow-up period had undergone re-revision. The cumulative one-year and five-year patient survival rate following ARMD revision was 99.4% (95% CI 99.1 to 99.7) and 95.9% (95% CI 92.3 to 97.8) respectively.

Re-revision surgery. Following ARMD revision, re-revision was performed in 192 hips (7.6%) at a mean of 1.2 years (one day to 5.7 years). In re-revised hips, 71 (37.0%) had more than one indication for failure. The most common re-revision indications were pain (n = 52, 27.1%), ARMD (n = 48, 25.0%), dislocation or subluxation (n = 43, 22.4%), infection (n = 31, 16.1%) and acetabular loosening (n = 29, 15.1%) (Table II).

The mean follow-up time for hips not undergoing re-revision was 2.9 years (1.0 to 6.6). The cumulative five-year implant survival rate following ARMD revision was 89.5% (95% CI 87.3 to 91.3) (Fig. 1).

Predictors of re-revision surgery: univariable analysis. Univariable analysis identified six predictors of re-revision (Table III): high BMI at revision; primary THA (compared with HR); shorter interval between primary and revision surgery; modular component only revisions (femoral head and liner with or without taper adapter); ceramic-on-ceramic revision bearings and acetabular bone grafting.

Predictors of re-revision surgery: multivariable analysis. The final multivariable model included 1766 hips (70% of the cohort) with data available for all variables, including BMI. Four predictors from the univariable analysis remained significant predictors of re-revision in the multivariable model (Table III): high BMI at revision (subhazard ratio (SHR) 1.06 per kg/m^2 increase; 95% CI 1.02 to 1.09; p = 0.001); modular component only revisions (SHR 2.01; 95% CI 1.19 to 3.38; p = 0.009); ceramic-on-ceramic revision bearings (SHR 1.86; 95% CI 1.23 to 2.80; p = 0.003); acetabular bone grafting (SHR 2.10; 95% CI 1.43 to 3.07; p < 0.001). Type of primary joint arthroplasty (THA *versus* HR) was not eligible for final model inclusion (p = 0.670). Time between primary and revision surgery was included in the final model, but did not reach statistical significance (p = 0.067). The final multivariable model had a reasonable discriminatory ability for distinguishing between hips undergoing and not undergoing re-revision

Table III. Univariable and multivariable Fine and Gray[12] competing-risk (mortality) regression analysis to identify predictors of re-revision surgery following revision surgery performed for adverse reactions to metal debris (ARMD)

Covariate	Univariable subhazard ratio (95% CI)	p-value	Multivariable subhazard ratio (95% CI)	p-value
Gender				
Female *vs* male	1.14 (0.85 to 1.55)	0.382	†	
Age at revision (per yr)	0.99 (0.98 to 1.01)	0.455	†	
BMI (per kg/m²)	1.05 (1.02 to 1.08)	**0.003**	1.06 (1.02 to 1.09)	**0.001**
Bilateral revisions for ARMD	1.03 (0.63 to 1.70)	0.901	†	
Primary hip arthroplasty				
HR	1.00	Ref	†	
THA	1.47 (1.05 to 2.06)	**0.023**		
Time from primary to revision (per yr)	0.87 (0.79 to 0.95)	**0.002**	0.91 (0.81 to 1.01)	0.067
ASA grade at revision				
1	1.00	Ref	1.00	Ref
2	1.00 (0.69 to 1.45)	0.989	*	0.946
3 or above	0.92 (0.50 to 1.70)	0.798	0.58 (0.28 to 1.21)	0.147
VTE – chemical				
None	1.00	Ref	†	
LMWH (+/-other)	0.66 (0.42 to 1.04)	0.074		
Aspirin only	0.87 (0.35 to 2.12)	0.753		
Other	0.72 (0.45 to 1.15)	0.173		
VTE – mechanical				
Any *vs* none	0.79 (0.39 to 1.60)	0.509	†	
Number of ARMD hip revision procedures performed by each centre (per 10 cases)	1.02 (0.99 to 1.05)	0.118	1.03 (0.99 to 1.06)	0.056
Revision surgeon grade				
Consultant *vs* other	0.83 (0.42 to 1.62)	0.583	†	
Surgical approach				
Posterior *vs* other	0.91 (0.63 to 1.32)	0.624	†	
Revision indications				
ARMD only	1.00	Ref	†	
2 to 6 indications	0.80 (0.58 to 1.09)	0.156		
Revision details				
Acetabular component (+/- head +/- liner +/- taper adapter)	1.00	Ref	1.00	Ref
All components revised	0.78 (0.56 to 1.07)	0.126	*	0.878
Femoral component (+/- head +/- liner +/- taper adapter)	0.22 (0.30 to 1.59)	0.133	‡	‡
Modular components only§	1.59 (1.04 to 2.43)	**0.032**	2.01 (1.19 to 3.38)	**0.009**
Revision femoral head size				
< 36 mm	1.00	Ref	†	
36 mm	1.12 (0.82 to 1.53)	0.491		
> 36 mm	1.04 (0.53 to 2.02)	0.915		
Revision bearing surface				
CoP	1.00	Ref	1.00	Ref
CoC	1.54 (1.10 to 2.16)	**0.013**	1.86 (1.23 to 2.80)	**0.003**
MoP	1.44 (0.98 to 2.10)	0.062	1.45 (0.88 to 2.39)	0.141
CoM, MoM or MoC	‡	‡	‡	‡
Acetabular component fixation				
Cementless	1.00	Ref	†	
Cemented	0.89 (0.54 to 1.47)	0.656		
Femoral component fixation				
Cementless	1.00	Ref	†	
Cemented	0.76 (0.44 to 1.30)	0.316		
Bone graft (femoral)	0.74 (0.28 to 1.96)	0.541	†	
Bone graft (acetabular)	1.52 (1.10 to 2.11)	**0.011**	2.10 (1.43 to 3.07)	**< 0.001**

*specific subgroup did not meet inclusion criteria for final multivariable model (p > 0.200)
†covariate was not eligible for inclusion in the final multivariable model
‡unable to calculate value as no hips in this subgroup underwent re-revision surgery
§involves revision of the femoral head and liner, with or without the use of a taper adapter
All univariable analyses were based on a cohort of 2416 hips with complete data available for all variables, excluding BMI (181 hips undergoing re-revision surgery and 39 deaths)
Multivariable analysis, and the univariable analysis for BMI were based on a cohort of 1766 hips with data available for all variables, including BMI (132 hips undergoing re-revision surgery and 28 deaths)
Statistically significant differences between the re-revised and non re-revised hips (p < 0.05) are highlighted in bold text
CI, confidence interval; BMI, body mass index; THA, total hip arthroplasty; HR, hip resurfacing; ASA, American Society of Anesthesiologists; VTE, venous thrombo-embolism; LMWH, low molecular weight heparin; CoP, ceramic-on-polyethylene; CoC, ceramic-on-ceramic; MoP, metal-on-polyethylene; CoM, ceramic-on-metal; MoM, metal-on-metal; MoC, metal-on-ceramic; Ref, reference group

surgery (c statistic = 0.66). When using the imputed dataset, high BMI at revision, modular component only revisions, ceramic-on-ceramic revision bearings and acetabular bone grafting were also identified as significant predictors of re-revision (supplementary table available online).

Modular component only revisions had an increased risk of re-revision compared with hips undergoing all component revisions (SHR 2.03; 95% CI 1.17 to 3.54; p = 0.012), and compared with hips undergoing acetabular component revisions (with or without head, liner, taper adapter revision) (SHR 2.01; 95% CI 1.19 to 3.38; p = 0.009). Re-revisions following modular component only revisions (n = 30) were most frequently for dislocation or subluxation (n = 10, 33.3%) and infection (n = 8, 26.7%). Ceramic-on-ceramic revision bearings had an increased risk of re-revision compared with hips revised with ceramic-on-polyethylene bearings (SHR 1.86; 95% CI 1.23 to 2.80; p = 0.003), but not compared with hips revised with metal-on-polyethylene bearings (SHR 1.27; 95% CI 0.80 to 2.02; p = 0.308). Re-revisions following the use of ceramic-on-ceramic revision bearings (n = 74) were most frequently for pain (n = 25, 33.8%), ARMD (n = 20, 27.0%) and acetabular loosening (n = 16, 21.6%).

Discussion

We observed few intra-operative complications during revision surgery for ARMD (1.6%). Similar to previous studies, fractures of the femur represented the most common complication.[16] Mortality rates following ARMD revision were

also low (4.1% at five years), which is lower than for primary THA according to NJR data (9.5% at five years).[9] However, this is likely to be related to the younger age of MoMHA patients undergoing revision surgery compared with the full population of primary THA patients (mean age 63.6 years *versus* 69 years, respectively).[9]

Early studies reported catastrophic short-term outcomes following ARMD revision, with one-third of patients requiring re-operations.[1,2,17] Recent studies have observed better outcomes with increased surgical experience,[8] with a reported five-year implant rate of survival of 87.9% following ARMD revision.[7] Although the five-year implant rate of survival was similar in our study (89.5%) to recent studies,[7,8] these outcomes appear inferior compared with the implant survival following revision of conventional THA performed at specialist centres.[18,19] However, registries may under report arthroplasty failures,[20,21] which makes comparison with single-centre cohorts problematic. Perhaps the fairest comparison of our results would be with registry outcomes following non-MoMHA revision. Although the lack of a comparator group undergoing non-MoMHA revision surgery is a significant limitation of our study, the NJR does report implant survival following such procedures.[9] The five-year implant survival rates following all-cause non-MoMHA revision surgery (with linked primary procedures) recorded in the NJR are 87.8% to 89.1% for primary metal-on-polyethylene THAs (depending on the method of fixation), and 88.2% for primary uncemented ceramic-on-ceramic THAs.[9] Therefore implant survival rates following MoMHA revision for ARMD appear similar to those in non-MoMHA patients revised for all indications. However it was not possible to adjust for potential confounding factors, given the non-MoMHA revision outcome data were obtained from the latest NJR report.[9] Furthermore, as most patients who underwent MoMHA were young and active,[22] consideration should be given to patient-reported outcome measures following revision but these were not available. Registries do not collect data on patient-reported outcomes following revision, or on non-revision procedures.[9]

Re-revisions following ARMD surgery occurred early, with the indications for re-revision similar to previous reports.[3] Dislocation can occur as the soft-tissue destruction of ARMD may require extensive debridement, and the diameter of the femoral head is commonly reduced.[2,8] The risk of infection is increased by repeat surgery and incomplete excision of metal debris and necrotic tissue, whilst ARMD-induced osteolysis may lead to loosening of the acetabular component.[2,3] Recurrence of ARMD has been reported following revision,[3] and in this series ARMD was recorded in 25% of all re-revision cases. This is concerning given the short-term follow-up and exchange to non-MoM bearings in all hips.

The final multivariable model was only reasonable for distinguishing between those hips which either did or did not undergo re-revision surgery. Registry based models are unlikely to have much better discriminatory ability given they do not collect data on variables such as blood metal ion levels and the findings from imaging. However, our final model did provide four predictors of re-revision with large effect sizes.

High BMI at revision and acetabular bone grafting were both associated with an increased risk of future re-revision. We consider these to be largely non-modifiable risk factors. High BMI also predicts re-revision following revision THA performed for non-ARMD indications.[23,24] Patients who required acetabular bone grafting had twice the risk of re-revision. Bone grafting suggests a more complex reconstruction, which may be required because of ARMD-induced osteolysis and/or iatrogenic bone loss from the removal of well-fixed components.[5,7,8] Alternatively acetabular bone grafting may represent a modifiable risk factor if the reasons for the higher re-revision rates are related to this strategy being ineffective for managing ARMD-induced osteolysis compared with other reconstructive methods. Complications associated with bone grafts include infection, component migration and loosening, which can all require further surgery.[25]

Modular component only revisions and ceramic-on-ceramic revision bearings both predicted future re-revision, and represent modifiable surgical risk factors. Some surgeons advise retaining well-fixed and well-positioned components at revision for ARMD, with exchange of the modular components to non-MoM bearings.[2,26] Taper adapters are also recommended if tapers are not severely damaged.[2,27] Modular exchange is attractive, to prevent the morbidity associated with the removal of well-fixed components.[16,28] However, there is little evidence to support this approach.[2,27] We observed that modular component-only revisions had twice the risk of re-revision compared with all component revisions and acetabular component-only revisions. Failures following modular revision were commonly due to dislocation. This supports the evidence from previous studies employing this strategy,[2,27] suggesting hip stability is difficult to control after ARMD revision with modular component exchange alone. As component malposition represents an important risk factor for subsequent revision of THAs,[29,30] the failure to correct any component malposition would be expected to increase the risk of future revision. However, the NJR does not collect information on component positioning. It is hoped that future studies with detailed radiographic data available could investigate this further.

There is no consensus on which non-MoM bearing surface should be used when revising for ARMD. Ceramic bearings are popular because MoMHA revision patients are generally young and active.[2,5,6,8] However, we observed that ceramic-on-ceramic bearings have an 86% increased risk of re-revision compared with ceramic-on-polyethylene bearings. It is unclear why hard-on-hard ceramic bearings have inferior outcomes, with re-revision indications in this subgroup being consistent with the whole cohort. However,

our analysis is limited as we do not know the specific type of ceramic head implanted. Our findings that ceramic-on-polyethylene bearings have the lowest re-revision risk following ARMD revision complement the registry observations of a lower failure rate for this bearing surface in primary THA.[9,31]

Primary MoM THA has an inferior survivorship compared with HR, even when bearing surfaces from the same manufacturer are implanted.[9,32,33] We observed that in MoMHAs undergoing ARMD revision, the primary implant (THA *versus* HR) did not influence the future re-revision risk. Although limited evidence is available, previous studies have also not identified any difference in outcome following ARMD revision between THAs and HRs.[3,7]

The strengths of our study include the use of linked data from the largest arthroplasty registry in the world, which provides details of the primary MoMHA and all subsequent procedures. Furthermore, the assessment of an unselected population will reduce the likelihood of sampling bias. Therefore, we suspect our findings have good external validity and generalisability. Given the large number of re-revisions, our regression models were not over-fitted.

Nevertheless, registries have numerous potential limitations, which could affect our findings. The use of observational data means we cannot infer causality. Non-registry validation is therefore recommended. However, it would be difficult to achieve this with adequate statistical power as specialist centres perform relatively few ARMD revisions.[1-3,5,7,8,26] Another important limitation is that no large scale validation of the NJR has been performed. Recent studies to validate MoMHA retrievals using NJR data concluded that although revision rates may be underestimated, the completeness of data and accuracy of procedures which were recorded within the NJR were excellent.[20,21] Therefore we assume our study only involves a sample of all ARMD revisions actually performed, and the subsequent rate of failure may also be underestimated. However, details of the cases included are likely to be accurate.

A further limitation is that MoMHA revision rates vary both regionally and between surgeons.[9,31,34,35] Various centres and surgeons may have used different criteria for both diagnosing ARMD and performing revisions. The ARMD revisions analysed here are suspected to comprise a heterogeneous group, ranging from small collections around the arthroplasty and/or metallosis to large invasive and destructive lesions.[1,5,7,8] Furthermore, as the NJR does not collect histopathological data, it is possible that some MoMHAs truly revised for ARMD have been missed as they may have been recorded with different indications in the NJR. Conversely some ARMD revisions in this study may have been misdiagnosed intra-operatively and were revised for non-ARMD indications, such as infection.

Although our findings have been compared with data on all primary hips from the NJR report,[9] the lack of raw data means that we cannot determine how the predictors identified here (such as high BMI and acetabular bone grafting) influence outcomes following non-MoMHA revisions. Although missing data for some variables (namely BMI) could potentially affect the final model, our findings were confirmed when missing data were imputed (supplementary table available online). Further surgery represents an important outcome measure, but some procedures will not have been captured by the NJR, such as closed reductions of dislocations, debridement and washouts for infection and internal fixation for periprosthetic fractures. Finally, although we assessed the effect of primary MoM implant (THA *versus* HR) on re-revision rates, it was not possible to stratify the analysis further by implant manufacturer as we were not allowed access to this sensitive data by the registry and manufacturers.

Data from the largest arthroplasty registry in the world have demonstrated that the short-term risk of re-revision following MoMHA revision surgery performed for ARMD was comparable with that reported within the NJR following all-cause non-MoMHA revision.[9] However predictors of re-revision included factors that the surgeon can modify intra-operatively (type of revision procedure and bearing surface). Surgeons may therefore be able to reduce the rate of failure further following ARMD revision. Our findings may be useful when advising MoMHA patients about the risks associated with revision surgery for ARMD, and for making decisions regarding the type of hip reconstruction to perform.

Take home message:

- Factors predictive of re-revision following ARMD revision surgery included modifiable factors (type of revision procedure and bearing surface), which suggests that surgeons may reduce failure rates further following ARMD revision.

Supplementary material

A table showing the competing risk regression analysis in a complete dataset, where missing data were imputed, is available alongside the online version of this article at www.bjj.boneandjoint.org.uk

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H. G. Pandit: Study design, Data interpretation, Manuscript revision and approval.

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